REMARKS

A. Regarding the Amendments

Claims 1-19 were previously canceled. Claims 20-37 have been amended to claim the subject matter of the invention with greater particularity and specificity. After this amended has been entered, claims 20-47 will be pending. Amendments to claims merely clarify the language of claims and correct minor typographical errors mentioned by the Examiner.

Specifically, claims 20 now recites:

> "characterizing the target biomolecule by optically analyzing the same to determine the structural properties thereof."

This limitation is present in the original specification. See, page 22, lines 19-26; line 4; page 47, line 21 through page 48, line 17 of the PCT application.

Claim 37 now provides for using a plurality of candidate "agents of interest" and for " selecting the identifying agent based on the modulating capacity of each of the candidate agent." These limitations are disclosed in the original specification which teaches to identify "library members" that "display the ability to modulate the target biomolecule activity." See, page 25, lines 3-5, and page 25, lines 15-21.

Accordingly, it is respectfully submitted that no new matter has been introduced by the amendments.

Claim 29 has been amended to correct a minor informality, as required by the Examiner. Claim 29, as amended, now uses proper Markush terminology. With regard to allegedly defective declaration required by the Examiner in item 1 on page 2 of the Office Action, the Applicants respectfully point out that such requirement was made by the PTO previously and the new declaration was filed on May 2, 2002. The PTO issued

Notice of Acceptance on July 11, 2002, by which it informed the Applicants that all the items in the application were acceptable. A copy of this Notice is attached herewith for the Examiner's easy reference.

Claim 36 that was suggested by the Examiner to contain allowable subject matter (item 25, page 14 of the Office Action). Accordingly, claim 36 has been amended and is now presented in independent form as new claim 38 that includes all of the limitations of the base claim 20 and the intervening claim 26.

B. Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 21, 22, and 28 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly failing to particularly point out and distinctly claim the subject matter regarded as the invention (items 5-7 on page 3 of the Office Action).

Claims 21 and 22 have been amended as suggested by the Examiner. The Examiner's suggestions regarding amending these claims are gratefully acknowledged. With respect to claim 28, the Applicants respectfully disagree that claim 27 (parent claim of claim 28) does not recite a complex as mentioned by the Examiner (item 7, page 3 of the Office Action). Claim 27 depends on claim 26, and, ultimately, on claim 20. Claim 20 does recite a complex, as can be seen. Every limitation recited in claim 20 is also considered recited in claim 27. Therefore, the Applicants submit there is no need to amend claim 28 as the sufficient antecedent basis for the limitation "complex" is present in claim 27.

Accordingly, it is submitted that the 35 U.S.C. § 112, second paragraph, rejection does not apply. Reconsideration and withdrawal of the rejection are respectfully requested.

C. **Rejections Under 35 U.S.C. § 102 (b)**

Claims 20-22, 26, 31, and 37 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by U.S. Patent No. 5,478,729 to Van Atta et al. (item 11, page 5 of the Office Action). This rejection is respectfully traversed.

It is axiomatic that a valid rejection of a claim for anticipation by a reference requires that the reference explicitly or inherently describe all of the elements, limitations, and relationships recited in the claim. It is submitted that Van Atta et al. do not describe all the elements and limitations recited in each of claims 20 and 37, as amended.

Indeed, Van Atta et al. teach methods only for detecting the presence of a compound using immunochemical techniques, as well as the quantity of the compound, in particular, by chemically modifying an analyte and its homolog that is also present in the sample, followed by the immunochemical detection of the modified analyte using antibodies (See, abstract; col. 4, lines 7-8; col. 2, lines 18-20). More specifically, Van Atta et al. teach to modify cysteine and homocysteine that are mixed together in a sample and then to detect homocysteine (see, col. 8, lines 32-35).

Van Atta et al. do not disclose "characterizing the target biomolecule by optically analyzing the same to determine the structural properties thereof," as required by claim 20, as amended. Clearly, Van Atta et al. do not teach determining the structural properties of the target biomolecule, since they are only concerned with detecting homocysteine the structural properties of which are known. Nor is there any disclosure in Van Atta et al. directed to "selecting the identifying agent based on the modulating capacity of each of the candidate agent," as required by claim 37, as amended.

Therefore, Van Atta et al. fail to disclose every element of claims 20 and 37, and, therefore, is not a proper prior art reference under 35 U.S.C. § 102(b). Accordingly, each of claims 20 and 37 is patentably distinguishable over Van Atta et al. Each of claims 21,

22, 26, and 31 directly or indirectly depends on claim 20 and is considered patentable for at least the same reason. Withdrawal of the rejection and reconsideration are respectfully requested.

D. Rejections Under 35 U.S.C. § 102 (a)

Claims 20-28, 31-34, and 37 have been rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by Wilker et al. (Agnew. Chem. Int. Ed. 1999) (item 9, page 4 of the Office Action). This rejection is respectfully traversed.

This is also a rejection based on anticipation by reference. The same standard for a valid rejection, as described above, applies, i.e., the reference must explicitly or inherently describe all of the elements, limitations, and relationships recited in the claim. It is submitted that Wilker et al. do not describe all the elements and limitations recited in each of claims 20 and 37, as amended.

Specifically, Wilker et al. disclose substrates for delivery electrons and holes to active sites in proteins where it is difficult to access the active sites, and further describe spectroscopic detection of the complexes designed for rapid oxidation/reduction of the protein. Wilker et al. do not describe any analytic techniques directed to "characterizing the target biomolecule by optically analyzing the same to determine the structural properties thereof," as recited in claim 20, as amended.

Furthermore, Wilker et al. teach that camphor displaces the Ru-linked substrate in the (Ru-EB)-based complex, but there is no disclosure in Wilker et al. directed to "selecting the identifying agent based on the modulating capacity of each of the candidate agent," as required by claim 37, as amended.

Therefore, the Wilker et al. article fails to disclose every element of claims 20 and 37 and, accordingly, is not a proper prior art reference under 35 U.S.C. § 102(a). Accordingly, each of claims 20 and 37 is patentably distinguishable over Wilker et al.

Each of claims 21-28, and 31-34 directly or indirectly depends on claim 20 and is considered patentable for at least the same reason. Withdrawal of the rejection and reconsideration are respectfully requested.

E. Rejections Under 35 U.S.C. § 103 (a)

1. Claims 23-25, and 33 have been rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Van Atta et al. in view of U.S. Patent No. 5,478,729 to Gelboin et al. (item 15, page 7 of the Office Action). This rejection is respectfully traversed.

To establish a *prima facie* case of obviousness over a combination of references, the following three basic criteria must be met: (1) there must be some suggestion or motivation to combine the references as proposed by the Examiner; (2) there must be a reasonable expectation of success as a result of such combination; and (3) when all the references are combined, the combination must teach or suggest all of the claim limitations. The Applicants respectfully submits that none of the criteria has been satisfied in this case because the above-mentioned combinations of references fail to teach or suggest every limitation of claims 23-25, and 33.

Claim 20 recites the methods described above. As discussed above, Van Atta et al. fail to describe "characterizing the target biomolecule by optically analyzing the same to determine the structural properties thereof," as recited by claim 20. Nor is there any motivation or suggestion to modify the teachings of Van Atta et al. to arrive to the above-described limitation that is lacking.

Indeed, Van Atta et al. concentrate exclusively on detection of homocysteine, as discussed above, the structure of which is known and is provided in Van Atta et al. Clearly, there is no need in determining the structural properties of the homocysteine, because they are known. It is the detection of the presence of homocysteine, not determination of its structure, that is the subject matter of Van Atta et al.

Gebolin et al. fail to cure this deficiency of Van Atta et al. Gebolin et al. discuss using P450 as an analyte in an essay and detection by radioimmunoassay (col. 12, lines 18-20), but are silent with respect to analyzing the structural properties thereof.

Therefore, the combination of Van Atta et al. and Gebolin et al. fails to disclose or suggest every limitation of claim 20. Accordingly, it is respectfully submitted that claim 20 is patentably distinguishable over Van Atta et al. in view of Gebolin et al. Claims 23-25 and 33 depend on claim 20, and are allowable for at least the same reason. Reconsideration and withdrawal of the rejection are respectfully requested.

2. In addition, claims 27 and 28 have been rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Van Atta et al. in view of U.S. Patent No. 6,406,913 to Ullman et al. (item 16, page 7 of the Office Action). This rejection is respectfully traversed.

As discussed above, Van Atta et al. fail to describe "characterizing the target biomolecule by optically analyzing the same to determine the structural properties thereof," as recited by claim 20. Ullman et al. fail to cure this deficiency of Van Atta et al. Ulmann et al. discuss the assay methods using induced luminescence, and disclose that various dyes can be used as photosensitizers, including $Ru(bpy)_3^{2+}$ (col. 28, lines 40-41). The methods described in Ullman et al. are directed to methods for determining the presence of an analyte in a medium (abstract), but there is no description of the analysis of the structural properties of any target biomolecules, as required by claim 20, as amended.

Therefore, the combination of Van Atta et al. and Ullman et al. fails to disclose or suggest every limitation of claim 20. Accordingly, it is respectfully submitted that claim 20 is patentably distinguishable over Van Atta et al. in view of Ullman et al. Each of claims 27 and 28 depends on claim 20, and both are allowable for at least the same reason. Reconsideration and withdrawal of the rejection are respectfully requested.

3. Furthermore, claim 29 has been rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Wilker et al. in view of U.S. Patent No. 5,157,032 to Barton (item 17, page 8 of the Office Action). This rejection is respectfully traversed.

As discussed above, Wilker et al. do not teach using any analytic techniques for "characterizing the target biomolecule by optically analyzing the same to determine the structural properties thereof," as recited in claim 20, as amended. Barton fails to cure this deficiency. What is disclosed in Barton is using mixed ligand complexes and their use as compounds that can be bound to DNA. One such product, as taught by Barton, that can be tethered to DNA, can be photosensitizer $[Ru(phen)_2dppz]^{2+}$ (col. 45, line 18). Barton fails to teach any analytical method for determining the structural properties of any target biomolecules, as required by claim 20, as amended.

Therefore, the combination of Wilker et al. and Barton fails to disclose or suggest every limitation of claim 20. Accordingly, it is respectfully submitted that claim 20 is patentably distinguishable over Wilker et al. in view of Barton. Claim 29 depends on claim 20, and is considered allowable for at least the same reason. Reconsideration and withdrawal of the rejection are respectfully requested.

4. Furthermore, claim 29 has been rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Van Atta et al. in view of Barton (item 18, page 9 of the Office Action). This rejection is respectfully traversed.

Van Atta et al. and Barton teach what is described above. As discussed, neither reference teaches or suggests "characterizing the target biomolecule by optically analyzing the same to determine the structural properties thereof," as recited by claim 20. It is, therefore, submitted, the combination of Van Atta et al. and Barton fails to disclose or suggest every limitation of claim 20. Accordingly, it is respectfully submitted that claim 20 is patentably distinguishable over Van Atta et al. in view of Barton. Claim 29 depends on claim 20, and is considered allowable for at least the same reason. Reconsideration and withdrawal of the rejection are respectfully requested.

5. In addition, claim 30 has been rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Wilker et al. in view of U.S. Patent No. 5,696,157 to Wang et al. (item 19, page 9 of the Office Action). This rejection is respectfully traversed.

Wilker et al. teach what is described above and fails to teach "characterizing the target biomolecule by optically analyzing the same to determine the structural properties thereof," as recited in claim 20, as amended. Wang et al. fail to cure this deficiency. Wang et al. describe using 7-aminocoumarin as a fluorescent label (col. 1, lines 25-29). Thus, the method taught by Wang et al. can be used for detection of enzymes. Wang et al. are silent with respect to determining the structural properties of any target, as required by claim 20, as amended. Moreover, Wang et al. teach the compounds they disclose (including 7-aminocoumarin) are "useful for fluorescent labeling and detection" (col. 1, lines 5-6), failing to teach other possible use of the compounds, including their use for determining the structural properties of biomolecules.

Therefore, the combination of Wilker et al. and Wang et al. fails to disclose or suggest every limitation of claim 20. Accordingly, it is respectfully submitted that claim 20 is patentably distinguishable over Wilker et al. in view of Wang et al. Claim 30 depends on claim 20, and is considered allowable for at least the same reason. Reconsideration and withdrawal of the rejection are respectfully requested.

6. In addition, claim 30 has been rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Van Atta et al. in view of Wang et al. (item 20, page 10 of the Office Action). This rejection is respectfully traversed.

Van Atta et al. and Wang et al. teach what is described above. As discussed, neither reference teaches or suggests "characterizing the target biomolecule by optically analyzing the same to determine the structural properties thereof," as recited by claim 20. Nor is there any motivation to use the compounds disclosed in Wang et al. (e.g., 7-aminocoumarin) for such structural analysis because Wang et al. teach the use of these compounds as fluorescent markers for detection purposes and for no other purpose.

Accordingly, it is respectfully submitted, the combination of Van Atta et al. and Wang et al. fails to disclose or suggest every limitation of claim 20. Thus, claim 20 is patentably distinguishable over Van Atta et al. in view of Wang et al. Claim 30 depends on claim 20, and is allowable for at least the same reason. Reconsideration and withdrawal of the rejection are respectfully requested.

7. Furthermore, claim 32 has been rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Van Atta et al. in view of U.S. Patent No. 5,569,745 to Goodbody et al. (item 21, page 11 of the Office Action). This rejection is respectfully traversed.

Van Atta et al. teach what is described above. Goodbody et al. fail to cure the deficiencies of Van Atta et al. Goodbody et al. only teach using compounds with alkyl chains as linking groups in peptide-chelator conjugates (col. 4, lines 24-25). There is nothing in Goodbody et al. disclosing or suggesting that their compounds can be useful for determining structural properties of any target biomolecule.

It is, therefore, submitted, the combination of Van Atta et al. and Goodbody et al. fails to disclose or suggest every limitation of claim 20. Accordingly, it is respectfully submitted that claim 20 is patentably distinguishable over Van Atta et al. in view of Barton. Claim 32 depends on claim 20, and is considered allowable for at least the same reason. Reconsideration and withdrawal of the rejection are respectfully requested.

8. In addition, claim 34 has been rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Van Atta et al. in view of Gelboin et al. and further in view of U.S. Patent No. 5,506,251 to Thirugnanam (item 22, page 11 of the Office Action). This rejection is respectfully traversed.

As discussed above, the combination of Van Atta et al. and Gebolin et al. fails to disclose or suggest every limitation of claim 20. Thirugnanam fails to cure this deficiency. While disclosing the use of imidazole as a substrate (Col. 1, lines 41-42),

Thirugnanam neither teaches nor suggests that his compounds can be used for "characterizing the target biomolecule by optically analyzing the same to determine the structural properties thereof," as recited by claim 20.

Accordingly, it is respectfully submitted, the combination of Van Atta et al., Gebolin et al., and Thirugnanam fails to disclose or suggest every limitation of claim 20. Thus, claim 20 is patentably distinguishable over Van Atta et al. in view of Gebolin et al., and further in view of Thirugnanam. Claim 34 depends on claim 20, and is allowable for at least the same reason. Reconsideration and withdrawal of the rejection are respectfully requested.

9. In addition, claim 35 has been rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Wilker et al. in view of Wang et al., and further in view of Leung et al. (the article in Bioorganic and Medicinal Chemistry Letters) (item 23, page 12 of the Office Action). This rejection is respectfully traversed.

As discussed above, the combination of Wilker et al. and Wang et al. fails to disclose or suggest every limitation of claim 20. Leung et al. fail to cure this deficiency. While Leung et al. teach using 7-amino-4-methyl-6-sulfocoumarin-3 acetic acid fluorescent dye, there is nothing in Leung et al. teaching or suggesting that such compounds can be used for "characterizing the target biomolecule by optically analyzing the same to determine the structural properties thereof," as recited by claim 20. Therefore, the combination of Wilker et al., Wang et al., and Leung et al. fails to disclose or suggest every limitation of claim 20.

In addition, it is submitted that Leung et al. cannot be used against any claims of the present application, because the publication date of Leung et al. (September 1999) is later than the effective filing date of the present application (July 19, 1999 which is the filing date of the parent application USSN 60/144,488).

Based on the above, it is respectfully submitted that claim 20 is patentably distinguishable over Wilker et al. in view of Wang et al., and further in view of Leung et al. Claim 35 depends on claim 20, and is considered allowable for at least the same reason. Reconsideration and withdrawal of the rejection are respectfully requested.

10. Finally, claim 35 has been rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Van Atta et al. in view of Wang et al., and further in view of Leung et al. (item 24, page 13 of the Office Action). This rejection is respectfully traversed.

As discussed above, the combination of Van Atta et al. and Wang et al. fails to disclose or suggest every limitation of claim 20. Leung et al. fail to cure this deficiency. As also discussed above, Leung et al. are silent with respect to any methods that can be used for determining the structural properties of any biomolecule, as required by claim 20. Therefore, the combination of Van Atta et al., Wang et al., and Leung et al. fails to disclose or suggest every limitation of claim 20. In addition, as mentioned above, Leung et al. is not a proper reference due to its publication date being after the effective filing date of this application.

Accordingly, it is respectfully submitted that claim 20 is patentably distinguishable over Van Atta et al. in view of Wang et al., and further in view of Leung et al. Claim 35 depends on claim 20, and is considered allowable for at least the same reason. Reconsideration and withdrawal of the rejection are respectfully requested.

CONCLUSION

In view of the above amendments and remarks, reconsideration and favorable action on all claims are respectfully requested. If the Examiner would like to discuss any of the issues raised in the Office Action, Applicant's representative can be reached at (858) 677-1456. No fee is believed to be due in connection with the present amendment. In case any fee is due, Please charge additional claim fees, or make any credits, to Deposit Account 07-1896.

Respectfully submitted,

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